Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/ijt

Review Article

Controversies and current status of pre-emptive nephrectomy for asymptomatic failed renal allograft in the late post-transplant period

Tarun Javali [a], *Aneesh Srivastava* [b,*]

[a] *Post Doctoral Fellow, Department of Urology and Renal Transplantation, Sanjay Gandhi Post Graduate Institute of Medical Science, Rai Barielly Road, Lucknow, Uttar Pradesh 226014, India*

[b] *Professor, Department of Urology and Renal Transplantation, Sanjay Gandhi Post Graduate Institute of Medical Science, Rai Barielly Road, Lucknow, Uttar Pradesh 226014, India*

ARTICLE INFO

Article history:
Received 12 December 2013
Accepted 11 January 2014
Available online 23 January 2014

Keywords:
Pre-emptive allograph nephrectomy
Failed renal transplant
Renal transplantation

ABSTRACT

This review article focuses on the controversies and pros and cons of doing a prophylactic allograph nephrectomy in asymptomatic patients with previously failed renal transplant.

1. Introduction

Refinements in surgical technique and the availability of potent immunosuppressants have markedly improved short-term graft survival and reduced acute rejection rates in the last two decades. However graft survival in later time periods has improved only modestly.[1] Since the incidence of early graft loss has reduced, death with a functioning allograft and chronic allograft nephropathy have become the predominant etiologies of graft failure, and the need for dialysis after graft loss is ranked among the top five reasons for initiation of dialysis.[2] Approximately 50% of all cadaveric renal transplants and one-third of living donor renal transplants fail within 10 years of undergoing renal transplant.[3]Following primary transplant failure, patients fall into either one of the following two categories: permanent dialysis and unsuitable for re-transplantation or bridge dialysis awaiting re-transplant in the near future.

In the late post-transplant period, graft nephrectomy is usually performed when, along with the graft failure, the patient develops the graft intolerance syndrome, which is characterized by anemia, malaise, hematuria, pain, graft swelling, weight loss and diarrhea.[4] However, the management of asymptomatic grafts remains controversial. The objective of this review is, therefore, to discuss the controversies and pros and cons of routine elective allograft nephrectomy for ***asymptomatic chronically failed*** renal allografts.

* *Corresponding author*. Tel.: +91 9415011093.
E-mail address: aneesh892012@gmail.com (A. Srivastava).

2212-0017/$ – see front matter
http://dx.doi.org/10.1016/j.ijt.2014.01.007

2. Issues involved in advocating routine allograft nephrectomy in failed transplants

2.1. Morbidity and mortality of the procedure

The underlying principal factor fueling the debate of routine allograft nephrectomy is the often-cited morbidity and mortality of the procedure. Transplant nephrectomy has long been considered as a hazardous surgical endeavor. Morbidity and mortality rates have been previously quoted to the tune of 17–60% and 1.5–14% mainly due immunosuppression, comorbid conditions of the patients and technical difficulty of the procedure.[5] Complications were higher in the pre-cyclosporin era. With the widespread use of calcineurin inhibitors and lower doses of steroids, transplant nephrectomy has become a much safer procedure. Ganesh G et al did a comparative study of graft nephrectomy in precyclosporine and cyclosporine era and concluded that morbidity was significantly reduced in recent times.[6]However the limitation in all these studies is that they have failed to differentiate complication rates in patients undergoing graft nephrectomy for an emergent/symptomatic condition versus elective indication for a chronically failed asymptomatic allograft. Mazzucchi et al, in their paper on surgical complications of allograft nephrectomy noted that late failed graft nephrectomies carried a higher potential for serious complications, which could be explained by the higher grade of difficulty of this surgery, which is undoubtedly greater compared with nephrectomies in the early post-transplant period.[7] Similarly, the paper on allograft nephrectomy from our institute highlighted that early graft nephrectomy, though technically easy, is associated with systemic complications, while late graft nephrectomy is technically more demanding with relatively increased risk of vascular and visceral injuries.[8] Hence, the standard practice in most centers in dealing with patients with failed transplant is to leave the graft in situ, unless symptomatic. The potential advantage of this strategy is avoidance of surgery in an immunosuppressed patient who may recently have had an increase in the immunosuppressive dose in order to salvage a failing graft. These patients are then maintained on low-dose prednisolone with or without a calcineurin inhibitor and are subsequently managed similar to other patients with chronic kidney disease.

2.2. Benefit of residual graft function

The purported benefit of leaving a failed graft in situ is that these patients even if they require dialysis, the residual kidney function may produce just enough urine output with or without diuretic augmentation to lessen the burden of fluid restriction. Other than this, erythropoietin secretion, hydroxylation of calcidiol and phosphate balance are also put forth as reasons for retaining the failed graft. Multiple observational studies have highlighted the contribution of residual kidney function as an independent predictor of survival in dialysis patients (especially peritoneal dialysis), as well as patients who return to dialysis after a failed transplant.[9–12] However, patients who return to dialysis therapy after kidney transplant failure have a more rapid decline in residual kidney function, than those initiating dialysis therapy with native kidney disease.[13]

2.3. Benefits and drawbacks of continued immunosuppression

The price of maintaining a failed graft is the need for continued immunosuppressants and its attendant risks like bone marrow suppression, malignancy, infections and metabolic complications, which in turn may foster higher cardiovascular morbidity. There are both pros and cons in maintaining immunosuppression after graft failure. There are few papers addressing this critical issue. However, the study by Smak Gregoor et al[14] is relevant in the present context. They found increased morbidity and mortality rates in association with low-dose immunosuppression in patients retuning to dialysis after transplant failure. What is more, such therapy did not lead to fewer rejections in the chronically failed graft. Hence the authors proposed stopping immunosuppression in such patients. However, data from the study by Jassal et al suggest that there may be a survival advantage in maintaining patients on long-term immunosuppression even after they return to peritoneal dialysis after a failed transplant.[15] Naini et al[16] analyzed 85 patients in whom immunosuppression was stopped once they returned to hemodialysis after allograft failure. 74 patients remained stable without fever, hematuria or graft tenderness during a mean interval of 46.5 months of follow-up.

Messa et al[17] recently proposed that immunosuppression should be discontinued relatively rapidly upon return to dialysis, with immediate cessation of antiproliferative drugs and complete withdrawal of calcineurin inhibitors within 1–8 weeks. The variety of the proposed protocols reflects the absence of good evidence with respect to management of these patients and the need for randomized controlled studies, which in any case may be difficult to plan.

2.4. Chronic inflammatory state due to failed allograft

As a group, the patients who return to dialysis after a failed transplant have been shown to have worse outcomes when compared to age matched dialysis controls.[18,19] The exact causes of these high morbidity and mortality rates in this cohort of patients are not well known. A poor control of the chronic kidney disease complications, the persistence of a chronic inflammatory state due to failed graft and the lack of the protective effect of the functioning graft have been proposed as plausible reasons.[20] Lopez-Gomez et al demonstrated that failed renal transplant patients who return to hemodialysis experience erythropoietin resistance, hypoalbuminemia, malnutrition and have elevated plasma CRP, ferritin and ESR which was significantly worse than in hemodialysis patients who were transplant naïve.[21] These biochemical parameters have been known to be associated with poorer clinical outcome. This is not surprising, as these markers of a chronic inflammatory state have been linked to arteriosclerosis and increased cardiovascular morbidity even in the general population. An even more important finding of the Gomez study, which is specifically relevant to this review, is that the above hematologic, biochemical, and clinical parameters of patients